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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 April 2001 (03.04.01)	
International application No. PCT/GB00/02361	**Applicant's or agent's file reference** G.1344 PCT
International filing date (day/month/year) 15 June 2000 (15.06.00)	**Priority date** (day/month/year) 13 July 1999 (13.07.99)
Applicant MILUTINOVIC, Sandra, Ginette et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

01 February 2001 (01.02.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

GB0002361

Copy for the designated Office (DO/US)

PCT/GB00

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

HUDSON, Christopher, Mark
Eli Lilly and Company Limited
Lilly Research Centre
Erl Wood Manor
Windlesham, Surrey GU20 6PH
ROYAUME-UNI

Date of mailing (day/month/year)
04 January 2001 (04.01.01)

Applicant's or agent's file reference
G.1344 PCT

IMPORTANT NOTIFICATION

International application No.
PCT/GB00/02361

International filing date (day/month/year)
15 June 2000 (15.06.00)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address
ELI LILLY AND COMPANY LIMITED
Kingsclere Road
Basingstoke
Hampshire RG21 6XA
United Kingdom

State of Nationality:
State of Residence:
Telephone No.: 00 44 1276 853441
Facsimile No.: 00 44 1276 853306
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [X] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
HUDSON, Christopher, Mark
Eli Lilly and Company Limited
Lilly Research Centre
Erl Wood Manor
Windlesham, Surrey GU20 6PH
United Kingdom

State of Nationality:
State of Residence:
Telephone No.: 00 44 1276 853441
Facsimile No.: 00 44 1276 853306
Teleprinter No.:

3. Further observations, if necessary:
The agent in Box 2 was appointed by the common representative in Box 1. All further correspondances hould be sent to the agent.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

Authorized officer
Dorothée Mülhausen
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

PRITCHARD, Judith
ELI LILLY AND COMPANY LTD.
Lilly Research Centre
Erl Wood Manor
Windlesham
Surrey GU20 6PH
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	17.08.2001
Applicant's or agent's file reference G.1344 PCT	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02361	15/06/2000	13/07/1999

Applicant
ELI LILLY AND COMPANY LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Roche, S Tel.+49 89 2399-8031

PATENT COOPERATION TREATY

REC'D 21 AUG 2001
WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
G.1344 PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02361	15/06/2000	13/07/1999
International Patent Classification (IPC) or national classification and IPC C07C311/37		
Applicant ELI LILLY AND COMPANY LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01/02/2001	17.08.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Mercey, J Telephone No. +49 89 2399 8956

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02361

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

2-30	as originally filed			
1	as received on	30/07/2001	with letter of	27/07/2001

Claims, No.:

1-15	as received on	30/07/2001	with letter of	27/07/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
   see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 7, with respect to industrial applicability.

because:

   ☒ the said international application, or the said claims Nos. 7 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7,11-13
	No:	Claims	8-10,14,15
Inventive step (IS)	Yes:	Claims	1-7,11-13

	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-6,8-15
	No:	Claims	

2. Citations and explanations
see separate sheet

Re Item I

Basis of the report

The amendments filed with the letter dated 27/7/01 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT. The amendments concerned are the first, fourth and fifth compounds of the disclaimer in Claim 8, it appearing that said compounds do not belong to the state of the art, disclaimers only being allowed in order to overcome an accidental novelty destroying disclosure.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 7 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1 : DE-C-726386
D2 : WO-A-9313079
D3 : J. Med. Chem., 1992, 35(5), 847-58
D4 : WO-A-9304682

NOVELTY

The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of Claims 8-10, 14 and 15 is not new in respect of the prior art as defined in the regulations (Rule 64(1)-(3) PCT), the disclaimer in Claim 8 excluding compounds 51 and 57 of D2, but **not** those of D1 and D3.

Thus D1 discloses a compound according to present Claims 8-10, namely the product of Ex. 13, which is a compound of present formula (I) wherein R^1 is H, R^2 is methyl, R^3 and R^4 are **ethyl**, and the sulfonamide is at the 4-position. Said compound is described as being active against bacterial infections (cf. page 1, lines 26-36), and is thus also novelty destroying for present Claims 14 and 15.

D3 discloses two compounds according to present Claims 8 and 9, namely compounds 29h and 30h in Scheme III on page 851 (the preparations of which are described on pages 855 and 856), which are compounds of present formula (I) wherein R^1 and R^2, together with the nitrogen atom to which they are attached, form a carbocyclic group containing 5 carbon atoms fused to a substituted phenyl group, R^3 and R^4, together with the nitrogen atom to which they are attached, form a carbocyclic group containing 4 carbon atoms and a further nitrogen atom i.e. a piperazinyl group, and the sulfonamide is at the 4-position.

INVENTIVE STEP (Article 33(3) PCT)

In the light of D4, which teaches 4-arylpiperazines and 4-arylpiperidines as antipsychotic agents, the problem to be solved by the present invention may be regarded as the provision of compounds which modulate the activity of neuronal calcium channels for use in the treatment of CNS disorders.

The solution provided by the compounds of Claim 1 are the benzenesulphonamides of formula (I) substituted at the 3- or 4-position by an aminomethyl group. Said compounds differ from those of D4 in view of the fact that when R^1 and R^2, together with the nitrogen atom to which they are attached, form a carbocyclic group, this may be substituted by 1-3 methyl or ethyl groups only, whereas in D4, the corresponding heterocycle is always substituted by the group Ar. There is no suggestion, either in D4 or in any other cited art, that by modifying the D4 compounds in this way, compounds with neuronal calcium channel modulating activity may be obtained, such an activity not being disclosed in D4, nor in any of the other cited art. D1-D3 are irrelevant to the question of inventive step, the compounds of D2 and D3 falling under the present formula (I) of Claim 1 being disclosed therein as intermediates only, and the compound of D1 for use in bacterial infections. Hence the use of the compounds of formula (I) according to Claims 1-6, the method of Claim 7, and the novel compounds of Claims 11-13 are inventive.

INDUSTRIAL APPLICABILITY

For the assessment of the present Claim 7 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of

claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

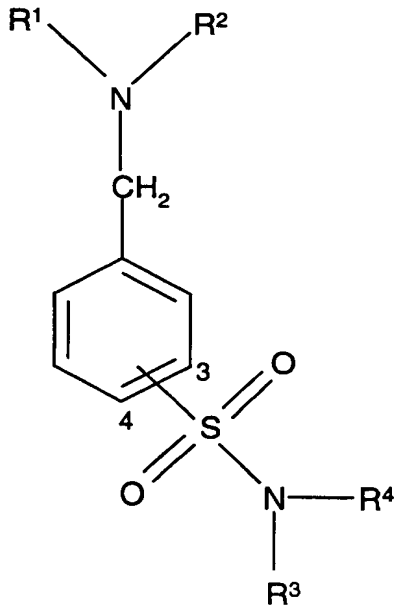
SULFONAMIDE SUBSTITUTED BENZYLAMINE DERIVATIVES AND THEIR USE AS MEDICAMENTS

This invention relates to novel chemical compounds and their use as pharmaceuticals.

It is well known that chemical compounds which modulate the activity of neuronal calcium channels are potentially useful in treating disorders of the central nervous system.

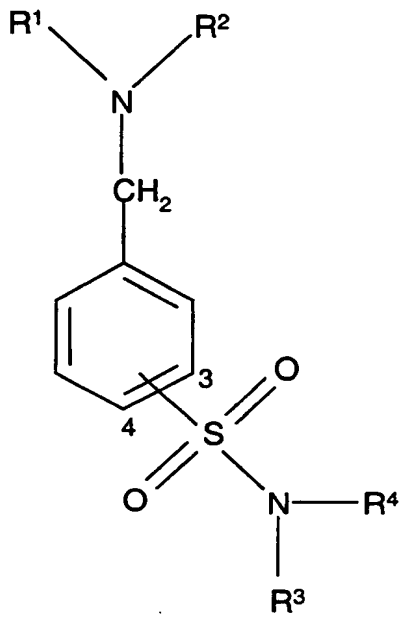
WO 93/04682 describes 4-arylpiperazines and 4-arylpiperidines useful for the treatment of disorders such as anxiety and aggression.

The compounds of the invention have the following general formula:



(I)

1. Use of a compound of the formula



(I)

in which the aminosulfonyl group is attached at the 3- or 4-position, and in which

R^1 is hydrogen, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl or optionally substituted phenyl-C_{1-4} alkyl,

R^2 is C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl, optionally substituted phenyl-C_{1-4} alkyl or $-(CH_2)_2NR^5R^6$ where R^5 and R^6 are each hydrogen or C_{1-6} alkyl, and

R^3 and R^4 are each C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl, C_{3-6} alkenyl, optionally substituted phenyl or optionally substituted phenyl-C_{1-4} alkyl,

or R^1 and R^2, or R^3 and R^4, or R^5 and R^6, together with the nitrogen atom to which they are attached, form a carbocyclic group containing 4 to 7 carbon atoms

optionally substituted with one to three methyl or ethyl groups and optionally containing an oxygen atom or a further nitrogen atom, said carbocyclic group being optionally fused to an optionally substituted phenyl group; or a salt thereof; for the manufacture of a medicament for treating a disorder of the central nervous system.

2. Use according to Claim 1 in which R^1, R^2, R^3 and R^4 are each C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl or optionally substituted phenyl-C_{1-4} alkyl, and R^1 can in addition be hydrogen, or R^1 and R^2, or R^3 and R^4 together with the nitrogen atom to which they are attached, form a carbocyclic group.

3. Use according to Claim 2 in which R^1, R^2, R^3 and R^4 are each C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl or optionally substituted phenyl-C_{1-4} alkyl, and R^1 can in addition be hydrogen.

4. Use according to Claim 3 in which R^1 is hydrogen, R^2 is optionally substituted phenyl-C_{1-4} alkyl and R^3 and R^4 are C_{1-6} alkyl.

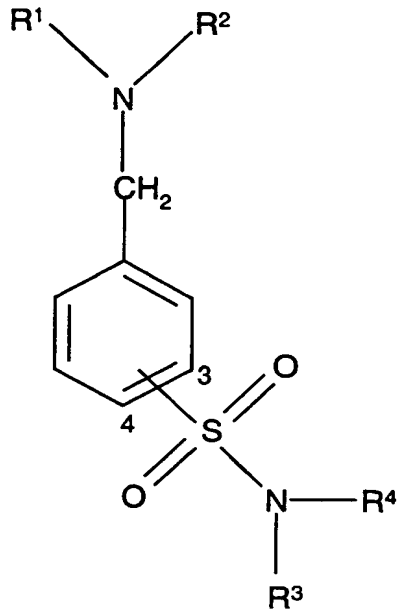
5. Use according to Claim 1 in which R^2 is $-(CH_2)_2NR^5R^6$.

6. Use according to Claim 1 or 5 in which R^3 or R^4 is C_{3-6} alkyl or when R^3 and R^4 are taken together with the nitrogen atom they form a piperidine ring which is substituted at the 3- and/or 5-positions with one or two methyl or ethyl substituents.

7. A method of treating a disorder of the central nervous system which comprises administering an effective

amount of a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof.

8. A compound of the formula



(I)

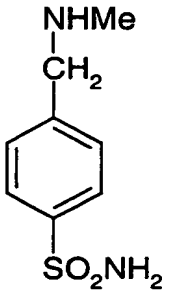
in which the aminosulfonyl group is attached at the 3- or 4-position, and in which

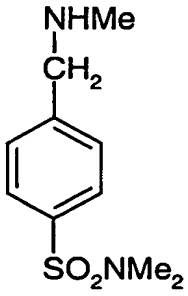
R^1 is hydrogen, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl or optionally substituted phenyl-C_{1-4} alkyl,

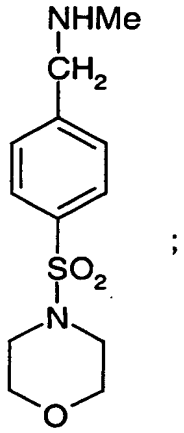
R^2 is C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl, optionally substituted phenyl-C_{1-4} alkyl or $-(CH_2)_2NR^5R^6$ where R^5 and R^6 are each hydrogen or C_{1-6} alkyl, and

R^3 and R^4 are each C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl, C_{3-6} alkenyl, optionally substituted phenyl or optionally substituted phenyl-C_{1-4} alkyl,

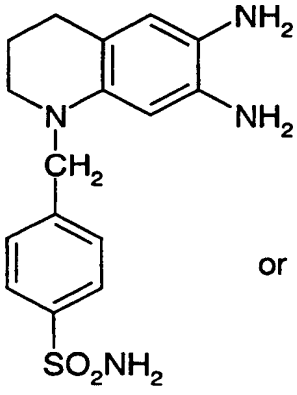
or R^1 and R^2, or R^3 and R^4, or R^5 and R^6, together with the nitrogen atom to which they are attached, form a carbocyclic group containing 4 to 7 carbon atoms optionally substituted with one to three methyl or ethyl groups and optionally containing an oxygen atom or a further nitrogen atom, said carbocyclic group being optionally fused to an optionally substituted phenyl group; or a salt thereof; with the proviso that said compound of formula (I) is not a compound of formulae:

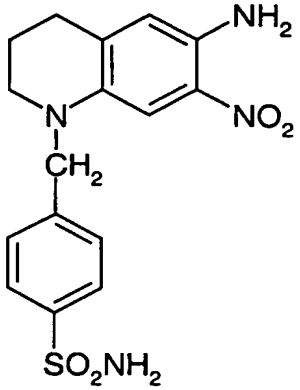


;


;


;



or


9. A compound according to Claim 1 in which R^1, R^2, R^3 and R^4 are each C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl or optionally substituted phenyl-C_{1-4} alkyl, and R^1 can in addition be hydrogen, or R^1

and R^2, or R^3 and R^4 together with the nitrogen atom to which they are attached, form a carbocyclic group.

10. A compound according to Claim 9 in which R^1, R^2, R^3 and R^4 are each C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl-C_{1-4} alkyl or optionally substituted phenyl-C_{1-4} alkyl, and R^1 can in addition be hydrogen.

11. A compound according to Claim 10 in which R^1 is hydrogen, R^2 is optionally substituted phenyl-C_{1-4} alkyl and R^3 and R^4 are C_{1-6} alkyl.

12. A compound according to Claim 8 in which R^2 is $-(CH_2)_2NR^5R^6$.

13. A compound according to Claim 8 or 12 in which R^3 or R^4 is C_{3-6} alkyl or when R^3 and R^4 are taken together with the nitrogen atom they form a piperidine ring which is substituted at the 3- and/or 5-positions with one or two methyl or ethyl substituents.

14. A pharmaceutical formulation comprising a compound according to any of Claims 8 to 13 or a pharmaceutically acceptable salt thereof, together with a diluent or carrier therefor.

15. A compound according to any of Claims 8 to 13, for use as a pharmaceutical.

INTERNATIONAL SEARCH REPORT

Inter Application No
PCT/GB 00/02361

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C311/37 C07D295/22 C07D295/12 C07D211/14 C07D213/38
C07D217/04 A61K31/18 A61K31/445

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 726 386 C (I.G. FARBENINDUSTRIE AG) page 1, lines 26-36; example 13	1-3,7,8
X	US 3 954 830 A (E.E. RENFREW ET AL) 4 May 1976 (1976-05-04) column 6, lines 28-29; column 10, lines 3-5, in combination with table I, examples 8, 18, 20, 29	1-3
X	WO 93 13079 A (AGOURON PHARMACEUTICALS INC) 8 July 1993 (1993-07-08) page 53, compound 51; page 57, compound 57	1-3
X	S.H. REICH ET AL: J. MED. CHEM., vol. 35, no. 5, 1992, pages 847-858, XP000953095 scheme III, compounds 29h, 30h	1

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 October 2000	07/11/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Van Amsterdam, L

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 93 04682 A (MCNEILAB INC) 18 March 1993 (1993-03-18) page 1, line 30 - page 2, line 14; table 4	1,2,6-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Application No
PCT/GB 00/02361

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
DE 726386	C		NONE		
US 3954830	A	04-05-1976	US	3858259 A	07-01-1975
			US	4008262 A	15-02-1977
			CA	1085843 A	16-09-1980
			JP	844174 C	15-02-1977
			JP	49023224 A	01-03-1974
			JP	51016208 B	22-05-1976
WO 9313079	A	08-07-1993	AU	3276793 A	28-07-1993
WO 9304682	A	18-03-1993	AU	1363392 A	05-04-1993
			AU	657799 B	23-03-1995
			AU	2659992 A	05-04-1993
			CA	2095826 A	12-03-1993
			CA	2095847 A	12-03-1993
			EP	0562049 A	29-09-1993
			EP	0563345 A	06-10-1993
			FI	932103 A	10-05-1993
			FI	932104 A	10-05-1993
			HU	217068 B	29-11-1999
			HU	64535 A	28-01-1994
			HU	68963 A	28-08-1995
			JP	2941945 B	30-08-1999
			JP	6502870 T	31-03-1994
			JP	6502183 T	10-03-1994
			KR	196249 B	15-06-1999
			MX	9102407 A	31-05-1994
			NO	303780 B	31-08-1998
			NO	931695 A	27-05-1993
			NZ	240863 A	27-04-1995
			PT	99700 A	31-03-1993
			RU	2139867 C	20-10-1999
			WO	9304684 A	18-03-1993
			US	5569659 A	29-10-1996
			ZA	9109629 A	06-12-1993